REMARKS

According to the Office Action mailed May 6, 2004, claims 1-16, 93-101, 106-136 and 138-180 are pending in the application. Claims 17-92, 102-105, 108-111, 134-137, 160-161, 163, 168, 172, 176, and 179-180 have been canceled without prejudice. Applicants reserve the right to prosecute the subject matter of the canceled claims in one or more divisional, continuation, and/or continuation-in-part applications. Claims 1, 162, 164, 165, and 166 have been amended to expedite issuance of the present application and without prejudice or disclaimer to pursuing the previously pending claims in a continuation application. Claims 5, 6 and 93 have been amended to correct clerical errors. Claims 181-194 have been newly added. Support for amended claim recitations can be found as follows:

Claim	Support
1	Page 27, lines 32-34; page 11, line 18; page 11, line 21; page 3, line 35
181, 182, 183, 184, 185, 186, 187, 188, 189	Page 27, lines 32-34; page 11, line 18
187	Page 32, lines 5-7
190, 191	Page 32, lines 1-7
192	Page 33, line 14 to page 34, line 19; page 36, line 10

Support for the recitation of at least 61, 92, 110, 116, and 122 different kinases can be found in the specification as follows. At page 27, lines 32-34, the specification teaches the identification of 122 protein kinases in the yeast genome. The specification teaches, *inter alia*, at page 11, lines 14-19, that the different proteins on an array of the invention can be 50% (*e.g.* 61 kinases of the 122 yeast kinases), 75% (*e.g.* 92 kinases of the 122 yeast kinases), 90% (*e.g.* 110 kinases of the 122 yeast kinases), or 95% (*e.g.* 116 kinases of the 122 yeast kinases) of all expressed proteins with the same type of biological activity in the genome of an organism.

Applicants note that "comprises" is intended to mean "consists of at least," and thus, the two terms are used interchangeably.

3. The Rejection Under 35 U.S.C. 112 Should Be Withdrawn

a. Written Description

Claims 1-11, 134-136, 141, 161, 164, 166, 169-170, 173-174, 177-178, and 180 were rejected under 35 U.S.C. 112, first paragraph for allegedly failing to meet the written description requirement. In the Office Action it is asserted that the disclosure is drawn to an array of yeast kinases, and therefore alleges that the specification does not sufficiently teach an addressable protein array wherein the protein has any type of activity and is from any organism. Furthermore, the Office Action alleges that the specification does not teach "50% of all expressed proteins with the same type of biological activity in the genome of an organism." The Office Action acknowledges that the specification adequately describes yeast kinases.

Without making any admissions as to the merits of the argument, Applicants have amended the claims to recite that the plurality of substances on the addressable array consists of at least 61 kinases or molecules comprising functional domains thereof of an organism selected from the group consisting of a mammal, yeast, and Drosophila. Accordingly, the phrase "50% of all expressed proteins with the same type of biological activity in the genome of an organism" is no longer recited in the claim. Furthermore, the type of biological activity is specified as kinase activity.

With respect to the organism from which the kinases originate, Applicants note that the claims have been amended to recite that the kinases are of an organism selected from a mammal, yeast, or Drosophila, and respectfully assert that the specification sets out sufficient detail to support using kinases from any species, including mammals, yeast, and Drosophila. The specification identifies that the organism can be, for example, a mammal, human or non-human animal, primate, mouse, rat, cat, dog, horse, cow, chicken, fungus such as yeast, Drosophila, bacteria, insects, and pigs (see *e.g.*, page 11, lines 19-22; and page 26, lines 28-30). Furthermore, it was well known as of the filing date of the pending application, that protein kinases catalyze protein phosphorylation and include conserved sequence motifs (Page 27, 27-31; and Hunter et al. TIBS, 22 (Jan. 1997), cited in Office Action). In addition, assays were available to determine and/or confirm kinase activity, and it was well known that kinases are well-conserved between species. For example, as illustrated in the present application, nearly all of the kinases that were identified using sequence analysis had kinase activity (Page 28, lines 12-14). Accordingly, Applicants respectfully assert that the

specification supports claims directed to protein arrays that include kinases from any species, and respectfully requests withdrawal of the rejection.

b. Enablement

Claims 1-11, 134-136, 141, 161, 164, 166, 169-170, 173-174, 177-178, and 180 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement. In the Office Action, it is asserted that the specification does not enable an addressable protein array wherein the protein has any type of activity and is from any organism. For example, the Office Action alleges that the specification does not provide a sufficient representative number of examples of proteins for organisms and of proteins of any type of activity. Furthermore, the Office Action alleges that the specification is silent as to how to determine whether proteins are 50% of all expressed proteins with the same type of biological activity in the genome of any organism.

Without making any admissions as to the merits of the argument, the claims have been amended to recite that the plurality of substances on the addressable array consists of at least 61 kinases or molecules comprising functional domains thereof of an organism selected from the group consisting of a mammal, yeast, and Drosophila. The phrase "50% of all expressed proteins with the same type of biological activity in the genome of an organism" is no longer recited in the claim. Furthermore, the claims recite that the proteins are kinases. Thus, the argument that the number of 50% of all expressed proteins cannot be predicted is moot.

With respect to the organism from which the kinases originate, Applicants note that the claims have been amended to recite that the kinases are of an organism selected from a mammal, yeast, or Drosophila. Applicants further respectfully assert that the specification combined with protein production methods known in the art, provide sufficient teaching to enable making and using arrays that comprise at least 61 kinases (or molecules comprising functional domains thereof) from a mammal, yeast, or Drosophila. Methods for expressing proteins, such as those disclosed in the specification, can be used to express kinases from any organism. The specification provides detailed methods for expressing eukaryotic kinases (Page 27, lines 3-17), and illustrates expression of yeast kinases, to show that protein expression methods known in the art can be used to express kinases for protein arrays. In fact, it has been confirmed that a baculovirus system, which is disclosed in the present specification (Page 27, lines 3-17), can been successfully employed to express human

proteins in the production of a protein chip that includes approximately 50 human kinases (see copending U.S. Application No. 10/865,431 filed June 9, 2004). In addition to the expression technologies disclosed in the specification, the spotting and immobilization technologies disclosed in the present application (see, *e.g.*, page 15, lines 1-15; page 16, line 15 to page 17, line 17; and page 30, lines 3-15) should be able to produce an array of expressed kinases from any species since kinases are all proteins and thus should be amenable to the same spotting and immobilization technologies to spot and immobilize any kinase.

Accordingly, Applicants respectfully assert that the specification enables the pending claims, which are directed to protein arrays that comprise kinases (or molecules comprising functional domains thereof) from a mammal, yeast, or Drosophila, and respectfully request withdrawal of the rejection.

4. The Rejection Under 35 U.S.C. 112 Second Paragraph Should Be Withdrawn

Claims 1-11, 134-136, 141, 161, 164, 166, 169-170, 173-174, 177-178, and 180 were rejected under 35 U.S.C. § 112, second paragraph, as allegedly failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Without making any admission as to the merits of the rejection, the claims have been amended to no longer recite percentages of all expressed proteins with the same type of biological activity. Accordingly the rejection has been overcome.

5. The Rejection Under 35 U.S.C. 103 Should Be Withdrawn

Claims 1-11, 134-136 and 161 were rejected under 35 USC 103(a) over Wagner et al. (U.S. Pat. No. 6,329,209; "Wagner").

Claim 1, from which the remaining claims depend, has been amended to recite that the positionally addressable array comprises a plurality of different substances, wherein the plurality of different substances on the addressable array consists of at least 61 kinases or molecules comprising functional domains thereof of an organism selected from the group consisting of a mammal, yeast, and Drosophila.

Even assuming *arguendo* that Wagner suggests the presently claimed protein arrays, Applicants assert that Wagner does not make the presently claimed arrays obvious because there is no reasonable expectation of success that the teachings of Wagner could be applied to

generate protein arrays with at least 61 kinases (or molecules comprising functional domains thereof) of an organism for reasons of record (see pages 7 to 8 of the Amendment Under 37 C.F.R. 1.111 filed April 10, 2003, which is incorporated herein by reference). Briefly, Wagner discloses arrays of protein-capture agents which can bind a plurality of proteins. Wagner fails, however, to teach protein-capture agents that could distinguish between at least 61 different protein kinases or molecules comprising functional domains thereof of an organism.

Claims 1-11, 134-136, 161, 164, 166, 173-174, 177-178, and 180 stand rejected under 35 USC 103(a) over Wagner et al. (U.S. Pat. No. 6,329,209) and Bielke et al. (Gene, 1994, 139(2):235-239).

Applicants respectfully disagree; Bielke fails to remedy the deficiencies of Wagner because Bielke fails to teach protein-capture agents that could be used in combination with the technology of Wagner to generate the presently claimed protein arrays. Thus, there is no reasonable expectation of success for the generation of protein arrays of the present invention in view of Bielke and Wagner.

Bielke describes the cloning of the human TSK-1 cDNA and the testis-specific expression of TSK-1 mRNA. Contrary to the statement in the Office Action that Bielke teaches a method of producing a kinase, Bielke describes the cloning and sequencing of the TSK-1 cDNA, but not recombinant expression of it. Bielke further uses a fragment of the TSK-1 cDNA to demonstrate the testis-specific expression of TSK-1 by Northern blot analysis.

Bielke does not suggest or teach how to express, isolate, and immobilize on an array at least 61 kinases of a yeast, mammal or Drosophila. In fact, Bielke does not even show that TSK-1 protein can be expressed from the clone. Furthermore, based on this shortcoming of Bielke, a skilled artisan would not be motivated to combine its teachings with those of Wagner et al.

6. Claims 1-11, 134-136, and 161 stand rejected under 35 USC 103(a) over Wagner et al. (U.S. Pat. No. 6,329,209) and Stern et al.

Claims 1-11, 134-136, and 161 were rejected as allegedly being obvious over Wagner and Stern et al. (Molecular and Cellular Biology, 1991, 11(2):987-1001).

The Office Action indicates that the array of Wagner et al. does not expressly include yeast protein kinases (Page 17, 2nd full paragraph). The Office Action cites Stern for teaching

the use of yeast protein kinases as a probe to be used on the arrays of Wagner. The Office Action alleges that one of ordinary skill in the art would have been motivated to use yeast protein kinases for use as a probe in the array of Wagner et al. for the advantage of providing an automated and/or miniaturized platform for an assay.

Stern uses a library filter blotting procedure to screen a yeast genomic library for proteins that are phosphorylated on tyrosine residues, to identify a gene encoding a tyrosine kinase. Applicants respectfully assert that Stern fails to remedy the deficiencies of Wagner because Stern, like Bielke, fails to teach protein-capture agents that could be used in combination with the technology of Wagner to generate the presently claimed protein arrays. Thus, there is no reasonable expectation of success for the generation of protein arrays of the present invention in view of Stern and Wagner.

7. **Rejection over Wagner et al. and Maskos et al.**

Claims 1-11, 134-136, and 161[1] were rejected as allegedly being obvious over Wagner and Maskos et al. (Nucleic Acids Research, 1992, 20(7):1679-1684). The Office Action states that Wagner does not expressly include the 3-glycidoxypropyltrimethoxysilane linker (GPTS). Instead, the Office Action alleges that the combination of Wagner and Maskos et al. renders the presently claimed invention obvious.

Maskos et al. is directed to nucleic acid synthesis on a glass support using GPTS, which is further derivatized to yield different linker molecules with different chain lengths. Applicants respectfully assert that Maskos fails to remedy the deficiencies of Wagner because Maskos fails to teach protein-capture agents that could be used in combination with the technology of Wagner to generate the presently claimed protein arrays. Thus, there is no reasonable expectation of success for the generation of protein arrays of the present invention in view of Maskos and Wagner.

In contrast to Maskos et al., the present invention describes the use of GPTS to immobilize proteins to a solid support. However, as the Examiner points out, the type of linker depends on the type of substrate and probe. Because Maskos et al. relates to the use of GPTS to immobilize nucleic acids and not proteins, there is no reasonable expectation of

[1] Even though the Office Action states that claims 134-136 and 161 are rejected over Wagner and Maskos, Applicants assume that the correct claims are 141 and 151 because these claims recite the 3-glycidoxypropyltrimethoxysilane linker that is the subject of the rejection over Wagner and Maskos.

success that GPTS can be used to immobilize proteins to a solid support to generate a positionally addressable protein array.

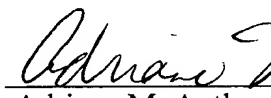
It is further argued in the Office Action that the skilled artisan would have been motivated to use the GPTS-derived linkers of Maskos for the arrays taught in Wagner because the linker is easy to synthesize and contains a hydroxyl functional group to bind with the probe. However, there are an unlimited number of compounds that include a hydroxyl functional group, and to select GPTS from this unlimited population of compounds is improper hindsight, especially considering that Maskos et al. discloses GPTS only in the context of nucleic acid synthesis. Thus, there is no motivation to combine Wagner with Maskos et al.

CONCLUSION

Applicants respectfully request that the amendments and remarks of the present response be entered and made of record in the instant application. Withdrawal of the Examiner's rejections and an allowance of the application are earnestly requested. If any issues remain in connection herewith, the Examiner is respectfully invited to telephone the undersigned to discuss the same.

Respectfully submitted,

Date: November 8, 2004



32,605
Adriane M. Antler (Reg. No.)

Jones Day
222 East 41st Street
New York, New York 10017
Telephone Number (212) 790-9090
Fax Nos.: (212) 869-9741/8864